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<u>L6</u>	13 and 15	18	<u>L6</u>
<u>L5</u>	11 and 14	19	<u>L5</u>
<u>L4</u>	immunosuppress\$	10829	<u>L4</u>
<u>L3</u>	11 and 12	25	<u>L3</u>
<u>L2</u>	mhc	4936	<u>L2</u>
<u>L1</u>	gp19k	37	<u>L1</u>

END OF SEARCH HISTORY

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-
- ☐ 1. 20020081707. 08 May 01. 27 Jun 02. Methods for helper-dependent adenoviral vector production. Armentano, Donna. 435/235.1; 435/320.1 435/325 536/23.72 C07H021/04 C12N007/01 C12N015/63 C12N005/02.
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- ☐ 2. 20020028194. 08 Aug 01. 07 Mar 02. Transgene expression systems. Kaplan, Johanne, et al. 424/93.21; 435/320.1 435/456 A61K048/00 C12N015/861.
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- ☐ 3. 20010008881. 06 Nov 98. 19 Jul 01. METHOD FOR THE AUGMENTATION OF GENE EXPRESSION. MOUNTZ, JOHN D., et al. 514/44; 424/130.1 435/320.1 435/325 514/2 A61K048/00.
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- ☐ 4. 6419919. 06 Nov 98; 16 Jul 02. Method for the augmentation of gene expression. Mountz; John D., et al. 424/93.2; 424/185.1 435/320.1 435/325 435/455 514/2 514/44 530/351. A01N043/04 A01N037/18 C12N015/63 A61K039/00 C07K001/00.
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- ☐ 5. 6399078. 01 Jun 99; 04 Jun 02. Chemokine--glycosaminoglycan complexes and their use in treating or preventing receptor mediated diseases. Devico; Anthony L., et al. 424/278.1; 424/185.1 424/279.1 514/2 514/56 514/59 514/885. A61K047/00 A61K039/00 A61K045/00 A61K038/00 A61K031/727.
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- ☐ 6. 6391632. 08 Oct 99; 21 May 02. Recombinant alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis. Dubensky, Jr.; Thomas W., et al. 435/325; 435/457 435/69.1 536/23.72. C12N005/10.
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- ☐ 7. 6376236. 22 Jan 99; 23 Apr 02. Recombinant alphavirus particles. Dubensky, Jr.; Thomas W., et al. 435/320.1; C12N015/63.
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- ☐ 8. 6372208. 28 Sep 99; 16 Apr 02. Method of reducing an immune response to a recombinant virus. Wilson; James M., et al. 424/93.2; 435/320.1 435/325 435/455 435/456 514/44. A61K048/00 C12N015/86.
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- ☐ 9. 6358507. 12 Oct 99; 19 Mar 02. Transgene expression systems. Kaplan; Johanne, et al. 424/93.2; 424/93.6 435/320.1 435/325 435/366 435/371 435/455 435/456 435/69.1 435/91.1 435/91.4 435/91.41 435/91.42. A61K048/00 C12N015/63 C12N015/861 C12N015/34.
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- ☐ 10. 6342372. 08 Jul 99; 29 Jan 02. Eukaryotic layered vector initiation systems for production of recombinant proteins. Dubensky, Jr.; Thomas W., et al. 435/69.1; 435/455 536/23.2 536/23.72 536/24.1. C12N005/16 C12N015/11 C12N015/33.
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- ☐ 11. 6287557. 21 Feb 96; 11 Sep 01. Methods of gene therapy using herpes viral vectors expressing GM-CSF. Bournsnel; Michael E. G., et al. 424/93.2; 435/320.1 435/455 435/91.4 435/91.41 435/91.42. A61K048/00 C12N015/88.
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- ☐ 12. 6251957. 22 Aug 97; 26 Jun 01. Method of reducing an immune response to a recombinant virus. Wilson; James M., et al. 424/85.2; 424/154.1 424/233.1 424/85.5 424/93.2 424/93.6 435/320.1
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435/325 435/455 435/456 435/465 514/44 514/49 514/50 514/885. A01N043/04 A61K031/70
C12N015/63 C12N015/00.

☐ 13. 6100086. 14 Apr 97; 08 Aug 00. Transgene expression systems. Kaplan; Johanne, et al.
435/320.1; 435/457 435/458 536/23.72 552/544. C12N015/86 C07J009/00.

☐ 14. 6020191. 14 Apr 97; 01 Feb 00. Adenoviral vectors capable of facilitating increased
persistence of transgene expression. Scaria; Abraham, et al. 435/320.1; 536/23.5. C12N015/86.

☐ 15. 6015694. 16 Sep 97; 18 Jan 00. Method for stimulating an immune response utilizing
recombinant alphavirus particles. Dubensky, Jr.; Thomas W., et al. 435/69.3; 424/199.1 424/204.1
424/228.1 424/234.1 424/265.1 424/274.1 424/277.1 536/23.5 536/23.7 536/23.72. C12P021/06.

☐ 16. 5981275. 14 Apr 97; 09 Nov 99. Transgene expression system for increased persistence.
Armentano; Donna, et al. 435/320.1; C12N015/00.

☐ 17. 5962318. 15 Nov 96; 05 Oct 99. Cytotoxic T lymphocyte-mediated immunotherapy. Rooney;
Cliona, et al. 435/325; 424/93.1 435/373 435/377. A01N063/00 C12N005/00.

☐ 18. 5872154. 24 Feb 95; 16 Feb 99. Method of reducing an immune response to a recombinant
adenovirus. Wilson; James M., et al. 424/154.1; 424/233.1 424/85.2 424/85.5 424/93.2 424/93.6 435/320.1
435/69.1 514/44 514/49 514/50. A61K038/00 A61K038/20 A61K038/21 A61K039/235.

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FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 17:08:21 ON 24 JUL 2002

L1 237313 S IMMUNOSUPPRESS?
L2 83 S GP19K
L3 10 S L1 AND L2
L4 4 DUP REM L3 (6 DUPLICATES REMOVED)
L5 330 S MHC-1
L6 0 S L2 AND L5
L7 117157 S MHC
L8 0 S L2 AND L6
L9 34 S L2 AND L7
L10 14 DUP REM L9 (20 DUPLICATES REMOVED)

=> d au ti so 1-14 l10

L10 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS
IN Kaplan, Johanne; Armentano, Donna; Gregory, Richard J.
TI Adenoviral vectors comprising a modified e4 region but retaining e4orf3
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2

L10 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
AU Wold, William S. M.; Tollefson, Ann E.
TI Adenovirus E3 proteins: 14.7K, RID, and gp19K inhibit
immune-induced cell death; adenovirus death protein promotes cell death
SO Seminars in Virology (1998), 8(6), 515-523
CODEN: SEVIEL; ISSN: 1044-5773

L10 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2002 ACS
AU Sparer, Tim E.; Gooding, Linda R.
TI Suppression of MHC class I antigen presentation by human
adenoviruses
SO Current Topics in Microbiology and Immunology (1998), 232(Antigen
Presentation), 135-147
CODEN: CTMIA3; ISSN: 0070-217X

L10 ANSWER 4 OF 14 MEDLINE
AU Bruder J T; Jie T; McVey D L; Kovesdi I
TI Expression of gp19K increases the persistence of transgene
expression from an adenovirus vector in the mouse lung and liver.
SO JOURNAL OF VIROLOGY, (1997 Oct) 71 (10) 7623-8.
Journal code: 0113724. ISSN: 0022-538X.

L10 ANSWER 5 OF 14 MEDLINE DUPLICATE 2
AU Schowalter D B; Tubb J C; Liu M; Wilson C B; Kay M A
TI Heterologous expression of adenovirus E3-gp19K in an Ela-deleted
adenovirus vector inhibits MHC I expression in vitro, but does
not prolong transgene expression in vivo.
SO GENE THERAPY, (1997 Apr) 4 (4) 351-60.
Journal code: 9421525. ISSN: 0969-7128.

L10 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2002 ACS
IN Bach, Jean-Francois; Chatenoud, Lucienne; Haddada, Hedi; Lee, Martin;
Perricaudet, Michel; Webb, Michelle
TI Therapeutic gene- and immunoprotective gene-containing recombinant

- adenovirus and immunosuppressive agent medicinal combination useful for
in vivo exogenic transfection and expression
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
- L10 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS
IN Lee, Martin; Perricaudet, Michel
TI Defective adenoviruses for gene therapy including a therapeutic gene and
a gene that protects transgenic cells from immune responses
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
- L10 ANSWER 8 OF 14 MEDLINE DUPLICATE 3
AU Basler C F; Droguett G; Horwitz M S
TI Sequence of the immunoregulatory early region 3 and flanking sequences of
adenovirus type 35.
SO GENE, (1996 May 8) 170 (2) 249-54.
Journal code: 7706761. ISSN: 0378-1119.
- L10 ANSWER 9 OF 14 MEDLINE DUPLICATE 4
AU Fejer G; Gyory I; Tufariello J; Horwitz M S
TI Characterization of transgenic mice containing adenovirus early region 3
genomic DNA.
SO JOURNAL OF VIROLOGY, (1994 Sep) 68 (9) 5871-81.
Journal code: 0113724. ISSN: 0022-538X.
- L10 ANSWER 10 OF 14 MEDLINE DUPLICATE 5
AU Wilson-Rawls J; Deutscher S L; Wold W S
TI The signal-anchor domain of adenovirus E3-6.7K, a type III integral
membrane protein, can direct adenovirus E3-**gp19K**, a type I
integral membrane protein, into the membrane of the endoplasmic
reticulum.
SO VIROLOGY, (1994 May 15) 201 (1) 66-76.
Journal code: 0110674. ISSN: 0042-6822.
- L10 ANSWER 11 OF 14 MEDLINE DUPLICATE 6
AU Hermiston T W; Tripp R A; Sparer T; Gooding L R; Wold W S
TI Deletion mutation analysis of the adenovirus type 2 E3-**gp19K**
protein: identification of sequences within the endoplasmic reticulum
luminal domain that are required for class I antigen binding and
protection from adenovirus-specific cytotoxic T lymphocytes.
SO JOURNAL OF VIROLOGY, (1993 Sep) 67 (9) 5289-98.
Journal code: 0113724. ISSN: 0022-538X.
- L10 ANSWER 12 OF 14 MEDLINE DUPLICATE 7
AU Hermiston T W; Hellwig R; Hierholzer J C; Wold W S
TI Sequence and functional analysis of the human adenovirus type 7 E3-
gp19K protein from 17 clinical isolates.
SO VIROLOGY, (1993 Dec) 197 (2) 593-600.
Journal code: 0110674. ISSN: 0042-6822.
- L10 ANSWER 13 OF 14 MEDLINE DUPLICATE 8
AU Rawle F C; Tollefson A E; Wold W S; Gooding L R
TI Mouse anti-adenovirus cytotoxic T lymphocytes. Inhibition of lysis by E3
gp19K but not E3 14.7K.
SO JOURNAL OF IMMUNOLOGY, (1989 Sep 15) 143 (6) 2031-7.
Journal code: 2985117R. ISSN: 0022-1767.

L10 ANSWER 14 OF 14 MEDLINE
AU Wold W S; Gooding L R
TI Adenovirus region E3 proteins that prevent cytolysis by cytotoxic T cells and tumor necrosis factor.
SO MOLECULAR BIOLOGY AND MEDICINE, (1989 Oct) 6 (5) 433-52. Ref: 145
Journal code: 8403879. ISSN: 0735-1313.

=> d bib 4-7 l10

L10 ANSWER 4 OF 14 MEDLINE
AN 97456530 MEDLINE
DN 97456530 PubMed ID: 9311844
TI Expression of **gp19K** increases the persistence of transgene expression from an adenovirus vector in the mouse lung and liver.
AU Bruder J T; Jie T; McVey D L; Kovesdi I
CS GenVec, Inc., Rockville, Maryland 20852, USA.. bruder@genvec.com
SO JOURNAL OF VIROLOGY, (1997 Oct) 71 (10) 7623-8.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971020

L10 ANSWER 5 OF 14 MEDLINE DUPLICATE 2
AN 97319619 MEDLINE
DN 97319619 PubMed ID: 9176522
TI Heterologous expression of adenovirus E3-**gp19K** in an Ela-deleted adenovirus vector inhibits **MHC** I expression in vitro, but does not prolong transgene expression in vivo.
AU Schowalter D B; Tubb J C; Liu M; Wilson C B; Kay M A
CS Department of Internal Medicine, University of Washington, Seattle 98195, USA.
NC DK49022 (NIDDK)
SO GENE THERAPY, (1997 Apr) 4 (4) 351-60.
Journal code: 9421525. ISSN: 0969-7128.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
ED Entered STN: 19970709
Last Updated on STN: 19970709
Entered Medline: 19970623

L10 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 1996:616318 CAPLUS
DN 125:238676
TI Therapeutic gene- and immunoprotective gene-containing recombinant adenovirus and immunosuppressive agent medicinal combination useful for
in vivo exogenic transfection and expression
IN Bach, Jean-Francois; Chatenoud, Lucienne; Haddada, Hedi; Lee, Martin; Perricaudet, Michel; Webb, Michelle
PA Rhone-Poulenc Rorer S.A., Fr.; Institut National De La Sante Et De La Recherche Medicale

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9625177	A1	19960822	WO 1996-FR218	19960212
	W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AZ, BY, KG, KZ, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2730411	A1	19960814	FR 1995-1662	19950214
	FR 2730411	B1	19970328		
	CA 2211039	AA	19960822	CA 1996-2211039	19960212
	AU 9647238	A1	19960904	AU 1996-47238	19960212
	AU 717218	B2	20000323		
	BR 9607310	A	19971125	BR 1996-7310	19960212
	EP 809516	A1	19971203	EP 1996-903080	19960212
	EP 809516	B1	20010822		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,				
SI	JP 11500430	T2	19990112	JP 1996-524707	19960212
	AT 204481	E	20010915	AT 1996-903080	19960212
	ES 2163612	T3	20020201	ES 1996-903080	19960212
	ZA 9601161	A	19960807	ZA 1996-1161	19960213
	FI 9703323	A	19970813	FI 1997-3323	19970813
	NO 9703724	A	19970813	NO 1997-3724	19970813
PRAI	FR 1995-1662	A	19950214		
	WO 1996-FR218	W	19960212		

L10 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2002 ACS

AN 1996:388336 CAPLUS

DN 125:50775

TI Defective adenoviruses for gene therapy including a therapeutic gene and a

gene that protects transgenic cells from immune responses

IN Lee, Martin; Perricaudet, Michel

PA Rhone-Poulenc Rorer S.A., Fr.

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9612030	A1	19960425	WO 1995-FR1326	19951011
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2725726	A1	19960419	FR 1994-12346	19941017
	FR 2725726	B1	19970103		
	CA 2201399	AA	19960425	CA 1995-2201399	19951011
	AU 9536584	A1	19960506	AU 1995-36584	19951011
	AU 712243	B2	19991104		

EP 787198	A1	19970806	EP 1995-934200	19951011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10507079	T2	19980714	JP 1995-512983	19951011
ZA 9508686	A	19960522	ZA 1995-8686	19951013
NO 9701590	A	19970407	NO 1997-1590	19970407
US 2002006395	A1	20020117	US 1997-817494	19970415
FI 9701613	A	19970416	FI 1997-1613	19970416
PRAI FR 1994-12346	A	19941017		
WO 1995-FR1326	W	19951011		

=> d ab 4 5 l10

L10 ANSWER 4 OF 14 MEDLINE

AB Activation of the cellular immune system and subsequent lysis of vector-transduced cells by adenovirus- or transgene-specific cytotoxic T lymphocytes have been shown to limit transgene expression in animal models. The adenovirus **gp19K** gene product associates with major histocompatibility complex class I proteins and prevents their maturation by sequestering them in the endoplasmic reticulum. **gp19K** has been shown to block the ability of adenovirus-specific cytotoxic T lymphocytes to recognize virus-infected cells in vitro. To determine if **gp19K** expression in an adenovirus vector would increase transgene persistence, a vector that replaces the E1 region of adenovirus with an expression cassette encoding both **gp19K** and beta-glucuronidase was constructed. This vector produced high levels of functional **gp19K** in infected cells. RNase protection analysis revealed efficient expression of the **gp19K** gene in the mouse lung. Enhanced persistence and increased beta-glucuronidase activity were observed in the lung and liver following delivery of the **gp19K**-expressing adenovirus vector in B10.HTG mice but not in BALB/c mice. Since **gp19K** binds to both class I alleles on B10.HTG mice but only one allele on BALB/c mice, these results suggest that the major histocompatibility complex class I haplotype of mice is important in determining the effectiveness of **gp19K** in vivo. Since **gp19K** has previously been shown to interact with every human major histocompatibility complex class I allele tested, the inclusion of **gp19K** in gene therapy vectors may increase vector persistence in human gene therapy trials.

L10 ANSWER 5 OF 14 MEDLINE

DUPLICATE 2

AB An Ela-deleted adenovirus vector constitutively expressing native adenovirus E3-**gp19K** (Ad.RSV-**gp19K**) was constructed in order to determine whether or not E3-**gp19K** mediated interference with antigen presentation would result in prolonged transgene expression in vivo. Cultured fibroblasts infected with Ad.RSV-**gp19K** produced a native size **gp19K** protein and had decreased cell surface levels of **MHC I** as shown by immunoprecipitation and flow cytometry. The congenic mouse strains Balb/b (H-2b **MHC I** with high **gp19K** affinity), Balb/k (H-2k **MHC I** with no **gp19K** affinity), and Balb/c (H-2d **MHC I** with moderate **gp19K** affinity) were chosen for in vivo experiments because of their range of **gp19K** affinities. Following transduction of mice from each strain with Ad.RSV-**gp19K** and Ad/RSV-hAAT (a reporter adenovirus), or Ad/RSV-cFIX (control adenovirus) and Ad/RSV-hAAT, the level and duration of serum hAAT protein were unrelated to **gp19K** protein expression. Evaluation of **MHC I** abundance on hepatocytes following in vivo transduction demonstrated that recombinant adenovirus rapidly increased the abundance of surface **MHC I** molecules on hepatocytes, and surface **MHC I** molecules were reduced earlier

and to a greater extent following wild-type adenovirus infection compared with hepatocytes transduced with control or Ad.RSV-gp19K recombinant adenovirus. This difference in surface MHC I down-regulation may be related to the different promoters (RSV-LTR versus the native E3 promoter) and will be an important consideration in the development of newer generation adenovirus vectors designed to evade host immune responses.

=> d bib 1 110

L10 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2002 ACS

AN 1998:712374 CAPLUS.

DN 129:311713

TI Adenoviral vectors comprising a modified e4 region but retaining e4orf3

IN Kaplan, Johanne; Armentano, Donna; Gregory, Richard J.

PA Genzyme Corp., USA

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9846779	A1	19981022	WO 1998-US7839	19980414
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6100086	A	20000808	US 1997-839679	19970414
	AU 9871335	A1	19981111	AU 1998-71335	19980414
	AU 727992	B2	20010104		
	EP 975785	A1	20000202	EP 1998-918408	19980414
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001524822	T2	20011204	JP 1998-544341	19980414
	US 6358507	B1	20020319	US 1999-416673	19991012
	US 2002028194	A1	20020307	US 2001-924925	20010808
PRAI	US 1997-839679	A	19970414		
	WO 1998-US7839	W	19980414		
	US 1999-416673	A1	19991012		

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FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 17:08:21 ON 24 JUL 2002

L1 237313 S IMMUNOSUPPRESS?
L2 83 S GP19K
L3 10 S L1 AND L2
L4 4 DUP REM L3 (6 DUPLICATES REMOVED)

=> d bib ab 1-4 l4

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:31619 CAPLUS
DN 134:95486
TI Recombinant adenovirus vectors expressing proteins with anti-cancer activity, and their use in treatment of cancer
IN Hermiston, Terry; Hawkins, Lynda K.; Johnson, Leisa
PA Onyx Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001002540	A2	20010111	WO 2000-US17856	20000630
	WO 2001002540	A3	20010830		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 2000060578	A5	20010122	AU 2000-60578	20000628
	EP 1218527	A2	20020703	EP 2000-946890	20000628
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
PRAI	US 1999-347604	A	19990702		
	WO 2000-US17856	W	20000630		
AB	The invention provides adenoviral shuttle vectors (pGE3SV, pGE3SV+V, pGE3SV+B and pGE3SV+V+B) that contain restriction sites in the E3 region which facilitates partial or total deletion of the E3 region or genes within the region. The E3 region contains genes encoding the 6.7K, gp19K, 10.4K, 14.5K, 14.7K and 11.6K proteins. The invention also provides a recombinant vector where the E3 region of the adenoviral shuttle vectors is replaced with a heterologous protein gene, where said gene is linked to a tissue-specific promoter. The invention further provides a recombinant vector where the E1A or E1b region of an adenoviral vector replaced with a heterologous protein gene. The heterologous protein is selected from a group consisting of tumor necrosis factor .alpha., interferon .gamma., an interleukin, a cell suicide protein, MIP-3 or a neg. selection protein, such as cytosine deaminase, or thymidine kinase. Finally, the invention provides cells transformed with said				

recombinant adenoviral vectors and use of said recombinant adenoviral vectors in treatment of cancer.

L4 ANSWER 2 OF 4 MEDLINE DUPLICATE 1
AN 2000305574 MEDLINE
DN 20305574 PubMed ID: 10845857
TI Second-generation adenoviral vectors do not prevent rapid loss of transgene expression and vector DNA from the arterial wall.
CM Comment in: Arterioscler Thromb Vasc Biol. 2000 Jun;20(6):1414-6
AU Wen S; Schneider D B; Driscoll R M; Vassalli G; Sassani A B; Dichek D A
CS Gladstone Institute of Cardiovascular Disease, University of California, San Francisco 94141-9100, USA.
NC HL 60504 (NHLBI)
P30 MH59047 (NIMH)
SO ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (2000 Jun) 20 (6) 1452-8.
Journal code: 9505803. ISSN: 1079-5642.
CY United States
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AB The utility of adenoviral vectors for arterial gene transfer is limited by the brevity of their expression and by inflammatory host responses. As a step toward circumventing these difficulties, we used a rabbit model of in vivo arterial gene transfer to test 3 second-generation vectors: a vector containing a temperature-sensitive mutation in the E2A region, a vector deleted of E2A, and a vector that expresses the immunomodulatory 19-kDa glycoprotein (**gp19k**) from adenovirus 2. Compared with similar first-generation vectors, the second-generation vectors did not significantly prolong beta-galactosidase transgene expression or decrease inflammation in the artery wall. Although cyclophosphamide ablated the immune and inflammatory responses to adenovirus infusion, it only marginally prolonged transgene expression (94% drop in expression between 3 and 14 days). In experiments performed with "null" adenoviral vectors (no transgene), loss of vector DNA from the arterial wall was also rapid (>99% decrease between 1 hour and 14 days), unrelated to dose, and only marginally blunted by cyclophosphamide. Thus, the early loss of transgene expression after adenoviral arterial gene transfer is due primarily to loss of vector DNA, is not correlated with the presence of local vascular inflammation, and cannot be prevented by use of E2A-defective viruses, expression of **gp19k**, or cyclophosphamide-mediated **immunosuppression**. Adenovirus-induced vascular inflammation can be prevented by cyclophosphamide treatment or by lowering the dose of infused virus. However, stabilization of adenovirus-mediated transgene expression in the arterial wall is a more elusive goal and will require novel approaches that prevent the early loss of vector DNA.

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1996:616318 CAPLUS
DN 125:238676
TI Therapeutic gene- and immunoprotective gene-containing recombinant adenovirus and **immunosuppressive** agent medicinal combination useful for in vivo exogenic transfection and expression

IN Bach, Jean-Francois; Chatenoud, Lucienne; Haddada, Hedi; Lee, Martin;
 Perricaudet, Michel; Webb, Michelle
 PA Rhone-Poulenc Rorer S.A., Fr.; Institut National De La Sante Et De La
 Recherche Medicale
 SO PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 DT Patent
 LA French
 FAN.CNT 1

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PI	WO 9625177	A1	19960822	WO 1996-FR218	19960212
	W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AZ, BY, KG, KZ, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2730411	A1	19960814	FR 1995-1662	19950214
	FR 2730411	B1	19970328		
	CA 2211039	AA	19960822	CA 1996-2211039	19960212
	AU 9647238	A1	19960904	AU 1996-47238	19960212
	AU 717218	B2	20000323		
	BR 9607310	A	19971125	BR 1996-7310	19960212
	EP 809516	A1	19971203	EP 1996-903080	19960212
	EP 809516	B1	20010822		
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SI JP 11500430 T2 19990112 JP 1996-524707 19960212
 AT 204481 E 20010915 AT 1996-903080 19960212
 ES 2163612 T3 20020201 ES 1996-903080 19960212
 ZA 9601161 A 19960807 ZA 1996-1161 19960213
 FI 9703323 A 19970813 FI 1997-3323 19970813
 NO 9703724 A 19970813 NO 1997-3724 19970813
 PRAI FR 1995-1662 A 19950214
 WO 1996-FR218 W 19960212
 AB A medicinal combination is disclosed which contains .gtoreq.1
immunosuppressive agent and .gtoreq.1 recombinant adenovirus with
 a genome that includes a 1st recombinant DNA contg. a therapeutic gene
 and
 2nd recombinant DNA contg. an immunoprotective gene, for consecutive,
 intermittent and/or simultaneous use in in vivo and/or ex vivo exogenic
 transfections. The methodol. of the invention provides protection of
 vectors and infected cells from the immune system, thereby preventing the
 rapid elimination of adenovirus from infected cells and prolonging
 expression of the virus-carried therapeutic gene.

L4 ANSWER 4 OF 4 MEDLINE DUPLICATE 2
 AN 96235144 MEDLINE
 DN 96235144 PubMed ID: 8666254
 TI Sequence of the immunoregulatory early region 3 and flanking sequences of
 adenovirus type 35.
 AU Basler C F; Droguett G; Horwitz M S
 CS Department of Microbiology and Immunology, Albert Einstein College of
 Medicine, Bronx, NY 10461, USA.
 NC 5T32 CA 09060 (NCI)
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 CA-13330 (NCI)
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 LA English
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 EM 199608
 ED Entered STN: 19960819
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 AB Adenovirus type 35 (Ad35) is an important pathogen in **immunosuppressed** individuals such as AIDS patients and bone marrow transplant recipients. Ad35, a member of Ad subgroup B, differs with respect to pathogenic properties from the more fully characterized subgroup C Ad, such as Ad2 and Ad5. One region of human Ad which varies between subgroups and which may influence Ad pathogenesis is early region 3 (E3), a region which appears to modulate the immune response to Ad infection. In order to begin to characterize the differences between the Ad35 E3 and the E3 of other Ad, the complete DNA sequence of the Ad35 E3 promoter and coding sequence along with two flanking structural proteins, pVIII and fiber, has been determined. Ad35 contains open reading frames which are unique to the subgroup B Ad in addition to the four characterized immunoregulatory proteins encoded by the subgroup C Ad. Further evaluation of the sequence of one of these proteins, 18.5K, which is the class-I major histocompatibility complex (MHC) binding protein of 18.5 kDa, demonstrates that the amino acid sequence of this Ad2 **gp19K** homologue fits a proposed model of **gp19K**-MHC interaction. Analysis of promoter sequences demonstrates that an NF-kappa B site found in the subgroup C E3 promoter is absent from the Ad35 E3 promoter. In addition, the fiber genes of Ad35 and other subgroup B Ad have been shown to diverge in an unexpected way, yielding three clusters of fiber homology.

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